3.0 OVERVIEW

Inhalation of asbestos dusts has been linked to several adverse health effects including primarily asbestosis, lung cancer, and mesothelioma (U.S. EPA 1986). Asbestosis, a chronic, degenerative lung disease, has been documented among asbestos workers from a wide variety of industries. Although asbestosis cases have been observed at some locations of current interest to the U.S. EPA, the disease is generally expected to be associated only with the higher levels of exposure commonly found in workplace settings and is not expected to contribute substantially to potential risks associated with environmental asbestos exposure. Therefore, asbestosis is only considered in this document to the extent required to address it's putative association with lung cancer. Overall, the majority of evidence indicates that lung cancer and mesothelioma are the most important sources of risk associated with exposure to low levels of asbestos.

> Note that the primary route of exposure of concern in association with asbestos is inhalation. There is little evidence that ingestion of asbestos induces disease (see, for example, U.S. EPA 1986, IRIS 1988). Therefore, this study is focused on inhalation hazards and other routes of exposure are not addressed.

Gastrointestinal cancers and cancers of other organs (e.g. larynx, kidney, and ovaries) have also been linked with asbestos exposures (by inhalation) in some studies. However, such associations are not as compelling as those for the primary health effects listed above and the potential risks from asbestos exposures associated with these other cancers are much lower (U.S. EPA 1986). Consequently, this document is focused on risks associated with the induction of lung cancer and mesothelioma.

A variety of human, animal, and tissue studies have provided insight into the nature of the relationship between asbestos exposure and disease. Ideally, human epidemiology studies are employed to determine the quantitative dose/response relationships and the attendant risk coefficients for asbestos exposure. Risk coefficients have been estimated for asbestos from approximately 20 epidemiology studies for which adequate dose-response data exist. Such factors vary widely, however, and the observed variation has not been reconciled. Among the objectives addressed in this study is to evaluate and account for the sources of uncertainty that contribute to the variation among the risk coefficients derived from the literature so that these estimates can be reasonably interpreted and recommendations for their use in risk assessment developed.

Animal and tissue studies indicate that asbestos potency is a complex function of several characteristics of asbestos dusts including fiber size and fiber type (i.e., fiber mineralogy). Moreover, the influence of fiber size is a complex function of both diameter and length as critical parameters (among others). Therefore, whenever the goal is to compare across samples with differing characteristics, it is not sufficient to

report asbestos concentrations simply as a function of mass (or any other single parameter) and this stands in stark contrast to the treatment of chemical toxins. It has generally been difficult to distinguish among the effects of fiber size and type in many studies because such effects are confounded and the materials studied have not been adequately characterized. However, several adequate studies do exist and these have been highlighted.

The influence of such effects cannot be adequately evaluated in the existing epidemiological studies because the analytical techniques used to monitor asbestos exposure in these studies are not capable of resolving all of the characteristics of asbestos dusts that other studies indicate are important. Moreover, the exposure indices (the range of structure sizes and shapes included in an analysis) that are employed in the existing epidemiology studies may not correspond precisely with the characteristics of asbestos that best relate to biological activity. This hinders the ability to compare the risk (dose-response) coefficients derived from the different studies. It also limits the confidence with which risk coefficients derived from the existing epidemiology studies can be applied to assess risks from asbestos exposure in other environments. Such limitations are explored in this study, along with potential remedies.

Based on the approach developed for evaluating asbestos-related cancer risk by the U.S. EPA (1986), risk is estimated as the product of a risk coefficient and a mathematical function that depends on the level of exposure, the duration of exposure, and time. The risk coefficient for lung cancer is generally denoted, "K_L" and the one for mesothelioma is "K_M."

A detailed description of both the lung cancer and mesothelioma models is provided in Chapter 6. The models differ depending on whether lung cancer or mesothelioma is being considered.

For lung cancer, the model estimates *relative* risk, which means that the increase in lung cancer incidence that is attributable to asbestos exposure is proportional to the background lung cancer incidence in the exposed population. The background cancer incidence is the rate of lung cancer that would be expected to occur in the population in the absence of asbestos exposure. In other words, background lung cancer incidence is the lung cancer rate for the exposed population that is attributable to all causes other than asbestos.

The model for mesothelioma is an *absolute* risk model. This means that the increase in mesothelioma attributable to asbestos is independent of the background rate of mesothelioma, which is negligible in the general population.

Ideally, the risk coefficients derived from the existing epidemiology studies could be combined with measurements from other exposure settings (using the corresponding models) to estimate lung cancer and mesothelioma risks in these other exposure settings. However, such risk estimates are only valid if both of the following conditions are met:

(1) asbestos is measured in the exposure setting of interest in the identical manner in which it was measured in the study from which the corresponding risk coefficients are derived; and

(2) such measurements reflect the characteristics of asbestos exposures that determine risk.

A growing body of evidence indicates that the way in which asbestos concentrations were measured in the existing epidemiology studies do not reflect the characteristics of asbestos exposure that determine risk. Therefore, measuring asbestos concentrations in the same way in exposure settings of interest may not be sufficient to assure validity of risk estimates derived using the published risk coefficients (and the corresponding models). This is because the second of the above-listed conditions would not be satisfied.

Considerations necessary to compare risk coefficients derived in different exposure settings (or to apply a coefficient to predict risk in a setting different from the one in which the coefficient was derived) have been elucidated clearly in a mathematical model (Chesson et al 1989). The consequences of the model indicate that adjusting the existing risk coefficients so that they reflect asbestos characteristics that determine biological activity requires knowledge of the fiber size distributions of the dusts studied in the *original* epidemiology studies. To the extent they exist, such data may be used to normalize each of the published risk coefficients so that they relate to a common exposure index reflecting asbestos characteristics that determine biological activity.

Among the goals of this evaluation is to assess the relative importance of such limitations and to attempt to construct “fixes” as appropriate (within the confines of the current state of knowledge). Consequently, we explored the possibility of defining an improved exposure index (that better reflects biological activity) and of applying such an improved index to the epidemiology data. We also evaluated improved ways of simultaneously accounting for the effects of both fiber size and type.

Unfortunately, some of the issues that need to be resolved to support development of a protocol for assessing asbestos-related risks cannot be entirely resolved with existing data. We have attempted to identify such issues, to assess their relative importance, and, when deemed appropriate, to propose limited and focused research projects designed to provide the data required to reduce the impacts of such knowledge gaps.